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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,314	09/22/2000	Mark Gurney	28341/6280NCP	1321

4743 7590 05/20/2003

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EXAMINER
TURNER, SHARON L

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/668,314	GURNEY ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-67,70 and 78* is/are pending in the application.

4a) Of the above claim(s) *70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-67 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *53-67,70 and 78* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed 10-28-02 has been entered into the record and has been fully considered.

2. The IDS filed 2-9-02 has been considered as indicated on the attached PTO-1449.

3. Claims 1-52, 68-69 and 71-77 are canceled. Claims 53-67, 70 and 78 are pending.

Election/Restriction

4. Applicants election of Group VII, claims 53-67 and 78 to the extent of the APP substrate and polypeptide of SEQ ID NO:2, residues 63-469, alpha secretase processing activity and substrate KLVFFAEDF with traverse is acknowledged.

Applicant's argue that the restriction requirement is onerous and unfair to applicants and the public, that there is no prima facie basis for restriction based upon an analysis of the relationships of the groups, that the restriction to molecular embodiments is improper, that species are appropriate to mutual exclusivity of the invention, that there is no search burden to the multiple inventions, that the inventions are related as genus and species and that the fragments share a portion of the full length sequence, and that the searches for multiple inventions are similar in nature. Applicants traverse the restriction between the multiple groups. In particular to elected group VII, applicants argue that groups II and VII are related as product and method of use and that the claims may be subject to rejoinder. Applicants argue that groups III, V and VII are related in that they involve screening assays with Asp1 activity even though the claims

differ with respect to particular recitations. Applicants argue that group VII and VIII are related in that group VIII is dependent upon claims in group VII and that the method of assaying would reveal related information to the method of treatment and that there is no serious search burden.

Applicant's arguments have been fully considered but are not persuasive. As set forth in the restriction requirement the basis for restriction is the presentation of applicant's claims which are drawn to multiple distinct compounds and methods. A prima facie case has been presented which is consistent with common US restriction practice, the MPEP and Office policy. In particular it is noted that paragraphs 8-11 addresses the multiplicity of relationships noted for the multiple product and process relationships. The claims further evidence such distinctness. Thus, the requirement is not believed to be onerous and unfair to applicants or to the public, but substantiated by the presentation of the claims. Restriction to molecular embodiments is proper as the claims delineate distinct compounds that are not commonly searchable. As previously set forth a proper species claim delineates shared structural and functional features, yet instant claims are not so related. As set forth there is a substantial search burden to the multiple inventions as the searches are not co-extensive in nature. Rejoinder is only appropriate upon indication of allowable subject matter and thus regrouping of particular inventions is not appropriate at this time. Similarly upon allowance of a generic claim, appropriate rejoinder may be considered as to properly submitted species claims. However, such is not appropriate at this time as there is no indication of allowable subject matter. Further, as previously set forth while particular groups may be related to

each other the required searches for each particular group are not co-extensive in nature and thus restriction is proper

It is noted that claim 70 is dawn to the substrate of claim 69 as amended on 6-11-02. Claim 70 was previously included in the invention group as the claim was written as dependent from claim 67. As amended it is clear that the dependency is to claim 69 and thus claim 70 is deemed to be drawn to a nonelected invention.

5. Claim 70 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 64 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 64 recites the limitation "wherein the detectable label" which is dependent upon claim 53. However, claim 53 lacks proper antecedent basis for this claim limitation.

Claim Rejections - 35 USC § 102 or 103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 53-64, 66, 67 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Bodovitz et al., J. of Neurochemistry, 64(1):307-315, 1995 as evidenced by ATCC catalog No. CRL-1573 or in the alternative under 35 U.S.C. 103(a) as obvious over Bodovitz et al., J. of Neruochemistry, 64(1):307-315, 1995 as evidenced by ATCC catalog No. CRL-1573.

Bodovitz et al., teach assay of alpha-secretase activity comprising the steps of contacting human embryonic kidney cells (HEK-293) with amyloid precursor protein. Bodovitz notes that iron is a molecule that modulates levels of APP metabolites including APP sol or C-terminal alpha-secretase derivative (C83) that are the products of alpha-secretase cleavage of the APP substrate, see in particular Abstract and p. 307, column 2, first paragraph. Bodovitz is silent as to whether or not the alpha secretase within the HEK293 cells is in fact hu-Asp1 of applicant's claims. However, it is noted that the HEK293 cell line is of human origin and thus the cell is considered to produce a human alpha-secretase that is a huAsp1. The USPTO has insufficient resources to determine whether or not the HEK293 alpha secretase is in fact huAsp1 of applicants claims and whether or not it comprises the noted sequence characteristics of claims 56-59 and 78. Thus, the Examiner has insufficient facts to determine whether the Bodovitz treatment is "inherently the same" or obvious as claimed since the examiner cannot

determine how the methods differ. Since the record does not allow the determination of if and how the claimed methods differ, the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Specifically, that the alpha secretase huAsp1 is or is not produced via the HEK 293 cells. Note the case law of In re Best 195 USPQ 430, 433 (CCPA 1977). Claims 54-55 and 60-61 recite product by process limitations, i.e., huAsp1 mad via recombinant methods. However, the novelty of the process lies in the product and not the steps used to produce it, see in particular MPEP 2113. Thus the Bodovitz alpha secretase/human aspartyl protease is sufficient to meet the process limitations. The Bodovitz teaches that the HEK293 cell is transfected to express APP751. Bodovitz is silent as to the sequence that is well known in the art as comprising the sequence LVFFAEDF and KLVFFAED as evidenced via the APP751 sequence noted in the specification as SEQ ID NO:57, see in particular residues 667-675 as claimed in claim 62. Bodovitz notes that the transfected cells were labeled as in claims 63-64with 50 uCi of radiolabel 35S methionine/cysteine as disclosed at p. 308-309, paragraph spanning, Radiolabeled immunoprecipitations. The measurement of alpha secretase cleavage includes measuring the production of amyloid alpha peptide (sAPPalpha) designated APP sol., by Bodovitz, see in particular Figures 2-4. The measurement is as a function/comparison of various iron levels and is therefore a comparison of either in the presence or the absence of inhibitor. Further Bodovitz notes that the alpha secretase cleavage is of benefit in comparison to beta secretase cleavage and teaches that such changes in iron and iron regulating proteins that shift cleavage to beta-secretase

pathways could contribute to Alzheimer's disease neurodegeneration. Thus, Bodovitz acknowledges that iron modulation in favor of the alpha secretase activity is one of benefit. Thus, Bodovitz acknowledges that modulators that increase alpha secretase activity are potentially beneficial to Alzheimer's patients as claimed. Thus, the reference teachings are deemed to anticipate the invention.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bodovitz

et al., J. of Neurochemistry, 64(1):307-315, 1995 as evidenced by ATCC catalog No. CRL-1573, Chyung et al., J. of Cell Biol., 138(3):671-80, Aug. 11, 1997 and Marx et al., Experimental Gerontol., 34(6):783-795, September 1, 1999.

Bodovitz et al., and ATCC catalog CRL-1573 set forth as above but do not teach an APP substrate with carboxy terminal di-lysine.

Chyung et al., and Marx et al., each teach carboxy terminal di-lysine modification of APP sustrates for the purpose of providing ER-retention signals such that intracellular compartmentalization of the substrate is achieved. Chyung and Marx teach the advantages of di-lysine modification in analysis of APP substrate cleavage based upon evidence that the intracellular cleavage more closely resembles actual beta amyloid processing cleavage in neuronal cell types as compared to cleavage in non-neuronal cells.

Thus, the skilled artisan would be motivated to modify the assay using the ER-retention signal to produce an assay that more closely resembles the natural site of APP processing in neuronal cells, but without introducing the difficulties of actually performing the assay in neuronal cell cultures that are difficult to isolate and maintain. One of skill in the art would have expected positive results utilizing such modification based upon the success of such system as reported by Chyung and Marx and the relative ease in making the modified peptides via either recombinant DNA technology or chemical synthesis. Thus the di-lysine substrate modification would be obvious to the skilled artisan.

Status of Claims

12. No claims are allowed.

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.

May 6, 2003

Gary L. Kunz

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